Web-Based Data Management Standards

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What is data management?

- Paper and electronic CRF design
- Database design & programming
- Data acquisition and entry into the database
- Data review (monitoring)
- Validation (cleaning)
- Coding and database finalization

It's the black box between interviewing the participant and handing over a file for statistical analysis.

The quality of the data management is directly related to the credibility of the study results.

Web-based Data Mgmt Standards

- ADAI DMC built for NIDA Clinical Trials Network (CTN)
  - ☐ Medication trials
  - ☐ Behavioral trials
  - ☐ Health services research
  - ☐ Surveys

Web-based Data Mgmt Standards

- CTN chose FDA compliant data management standards for the highest credibility of their data

    - Medication trials held to the highest data standards
    - FDA regulated
    - Clearly documented minimum *system* requirements

Web-based Data Mgmt Standards

"COMPUTERIZED SYSTEMS USED IN CLINICAL TRIALS" (dated 4/99) – part of Fed Regs

- ☐ U.S. DHHS, Food and Drug Administration
- ☐ Center for Biologic Evaluation and Research
- ☐ Center for Drug Evaluation and Research
- ☐ Center for Devices and Radiological Health
- ☐ Center for Food Safety and Nutrition
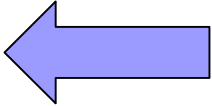- ☐ Center for Veterinary Medicine
- ☐ Office of Regulatory Affairs

Web-based Data Mgmt Standards

- Society for Clinical Data Management
  - □ "SCDM Good Clinical **Data Mgmt** Practices" (dated 9/03) – guidance document

  - □ "…the need for good clinical data mgmt practices has become even more important as…regulatory bodies rely more and more on the evaluation of electronically transmitted clinical trials data for critical data-based decision making."

Web-based Data Mgmt Standards

- Data Mgmt standards & guidelines focus on:
  - ☐ Data Acquisition ⬅
  - ☐ Data Entry
  - ☐ Data Audits
  - ☐ Data Storage
  - ☐ Database Closure (locking)
  - ☐ Data Archiving
  - ☐ Data Privacy
  - ☐ Documented Procedures (SOPs)

Data Acquisition Systems

- Web based
- Paper based
  - Teleforms – based on faxing
  - ClinTrials – bubble sheets
- Other types: Access, SPSS DE

Data Acquisition Systems

Why web based?

- Scalable

- Highly secure

- Study can be fully reproduced

  - Any and all changes to study database are recorded

- Greatest level of accountability to project

Data Acquisition System: WebData

- **System Requirements**
  - ☐ Internet Explorer 6.0, and above, with SSL packets permitted across LAN firewalls
  - ☐ 56K Modem, DSL or T1 line
  - ☐ Internet service
- **System Design**
  - ☐ SQL Server 2000 Database
  - ☐ dotnet-designed web interface

Data Acquisition System: WebData

- WebData is example of a web system compliant with recognized standards
- Custom designed for NIDA CTN
- Infrastructure to support simultaneous multi-site trials
- For use in any longitudinal study involving human subjects
- Survey research next

Data Acquisition Systems

- Main expenses for web systems occur during development

- Web applications
  - Programmer FTEs prior to launch (~4 months)

- Paper based applications
  - Data manager FTEs scale based on length of data collection phase, quantity of data)

Data Acquisition System: WebData

- DMC Infrastructure surrounding WebData:

  - ☐ Case Report Form (CRF) development
  - ☐ CRF Administration Instructions development
  - ☐ Data Dictionary (DD) development
  - ☐ Participant management assistance
    - What forms are/were administered when
  - ☐ > 60 standard data management reports for each project

Data Acquisition System: WebData

- Data Dictionaries are cornerstone of app
  - ☐ Form generator reads Excel DD
  - ☐ Creates data entry pages to mirror paper CRF
  - ☐ Creates SQL tables to house answers
  - ☐ Formatting customizations enabled
  - ☐ Custom messages enabled

Data Acquisition System: WebData

- Development/test modes
- Local software tester validates
  - Each CRF tested & debugged
  - Any custom features for the protocol
    - Blinded CRFs
    - Linked records (parent/child or physician/patient relationships)

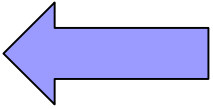# Data Acquisition System: WebData

- **Training mode**
  - All end users must be trained & certified by us
  - Assigned permissions after passing certification exam
  - All protocols have a practice area for the life of their protocol
    - New features can be introduced here prior to implementation in protocol
- **Production mode**
  - Real study data

Web-based Data Mgmt Standards

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  - Data Archiving
  - Data Privacy
  - Documented Procedures (SOPs)

Data Entry: WebData System

- No duplicate records are permitted into the system
- Access to CRFs can be based on permissions (protects blinding)
- On-line help system assists end users
- Integrated technical support requests

Data Entry: WebData System

- Front-end validation checks data as it is entered
  - Within range?
  - Correct data type?
  - Missing data
    - Confirmed missing code
  - Intra-CRF logic checks

Data Entry: WebData System

Automated ongoing data cleaning during data collection

- Support Desk 'back-end' checks
  - □ Data Managers conduct weekly data quality checks in SAS
  - □ Automated notification for end user if error found
  - □ Monitored resolution within 7 days

Data Entry: WebData System

Verify Mode:

- Double data entry of CRFs permits verification of up to 100% of data

- Discrepancies can be resolved with end user through Support Desk

Data Entry: WebData System
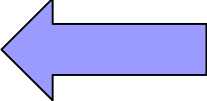
Data Management Reports
- Participant Recruitment, Progress & Retention
- Missing Forms
- Timeliness & Completeness of data
- Data Accuracy

By Site, by User ID, by randomization condition, by study

Permits early intervention with protocol problems

Web-based Data Mgmt Standards

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Data Audits: WebData System

- Quality Assurance department checks CRF to screen data quality
  - Legible?
  - Following edit procedures?
  - Proper coding?
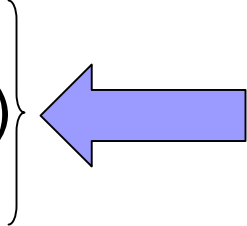- Double data entry – verifies screen to database accuracy

Data Audits: WebData System

- WebData audit trail monitors any changes to database
  - Date/time stamp, user ID for all activity
  - Data entry
  - Data edits (including reasons for change)
  - Data deletions limited to DMC staff after initial save to database
    - also recorded in audit trail
  - Programmer access to production data also audited

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- ☐ Documented Procedures (SOPs)

Data Storage, Closure & Archive

Data Storage

- Nightly backups for 30 days
- Weekly for 6 months
- Monthly for 1 year
- Stored in safe deposit box off campus

Data Storage, Closure & Archive

Database Closure & Archive

- Data is cleaned on ongoing basis
- No surprises at end of study
- No unexplained missing data
- Final queries can be resolved quickly
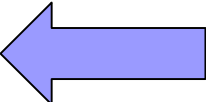- Database lock and archive in 2 months

Data Storage, Closure & Archive

Database Lock & Archive

- Once locked, your statistician is READY TO GO with clean data file

  ☐ Interim data files are available

- Copies of DDs provided with data set

- Archived copy retained at DMC for 7 years

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Data Privacy: WebData System

- Privacy and Security
  - FDA standards
  - Hipaa standards
- ADAI DMC intends full compliance with both

Data Privacy: WebData System

Privacy

- Participant identifiers determined on protocol by protocol basis
  - WebData can serve as master list
  - CRF design insures minimal identifiers in battery
- Data collected from other sources not protected until brought into WebData (e.g., hospital records)
- Evaluate 3rd party software for compliance

Data Privacy: WebData System

Privacy

- Only trained & certified users permitted in system
- All DMC staff trained on research ethics and Hipaa compliance
- Auto log-off after 15 minutes of inactivity
- Security of paper documents are responsibility of research staff
  - SOPs provided

Data Privacy: WebData System

Privacy

- Electronic transfer of data secured
  - □ Once in WebData, transmission mechanisms are secure
  - □ Have assisted protocols that require transmission of data outside of WebData (e.g., desktop apps)
- Access to data during data collection secured by permissions
- Who receives copies of database
  - □ Tracked by first person distribution

Data Privacy: WebData System

Privacy

- Each protocol obtains IRB approval for data handling

- DMC is submitting IRB application for WebData
  - Brings data management standards to IRB
  - Will speed IRB approval process for UW projects
  - Subcontracts for non-UW projects have IRB materials available for their local IRBs

Data Privacy: WebData System

Security

- Physical security of servers
  - ☐ Limited access, records entry to room
  - ☐ Servers distributed by function to minimize system interruptions
  - ☐ Backup tapes/disaster recovery plans in place
- Firewall

Data Privacy: WebData System

Security

- Authentication
  - Server: Digital certificates, HTTPS encryption
  - User: Logins required for each session/15 minute auto-log off when inactive
  - User: Strong passwords required to change every 4 months
  - Permissions assigned and rescinded by protocol based on PI and DMC Director
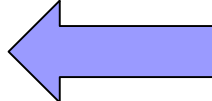
Data Privacy: WebData System

Security

- Data Transmission
  - SSL file transfer system for all data
- Data is NEVER emailed

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SOPs

- **All procedures documented**
  - ☐ Case Report Form & Data Dictionary development
    - ■ Includes missing data procedures
  - ☐ Data monitoring & cleaning after protocol launch
  - ☐ System development & disaster recovery procedures
  - ☐ Change control

- **Good documentation facilitates seamless work across projects and staff, minimizes errors within the DMC, creates reproducible study results, lends credibility to conclusions**

Formal Data Management Services

- Why bother?

Formal Data Management Services

- From SCDM Good Clinical Data Management Practices:

"The review & approval of new pharmaceuticals by federal regulatory agencies is contingent upon a trust that the clinical trials data presented are of sufficient integrity to ensure confidence in the results and conclusions presented by the sponsor company. To that same goal, companies must assure that all staff involved in the clinical development program are trained and qualified to perform those tasks for which they are responsible."

Formal Data Management Services

- Used in high profile studies (e.g., CTN)
- Required for services falling under federal regulations (e.g., medications). Health insurance next?
- IRBs becoming increasingly more conservative
- Manuscript preparation and review is improved by level of documentation
- Brings credibility, protects against allegations of misconduct

Formal Data Management Services

- Why no data mgmt standards in non-medical trials?

- Doesn't the quality of the data = the quality of the study?